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(71) Applicant *(for all designated States except US)*: PROVIVO AB [SE/SE]; Stortorget 13, S-211 22 Malmö (SE).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)* : ANDERSSON, Ralf [SE/SE]; Drottninggatan 156, S-252 33 Helsingborg (SE).

(74) Agent: AWAPATENT AB; Box 5117, S-200 71 Malmö (SE).

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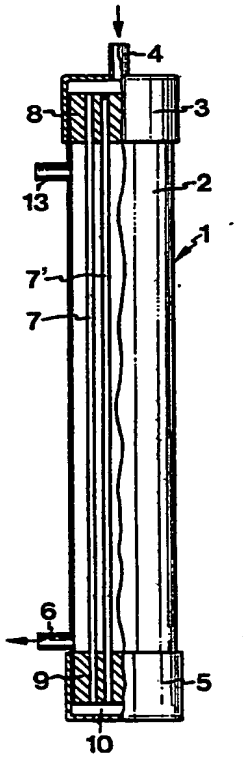
(57) Abstract

A disposable filter comprises a bundle of hollow fibres arranged in a housing having an inlet for a particle-laden volume of liquid to be filtered, as well as an outlet or a collecting chamber for the permeate. The inlet communicates with the interior of the hollow fibres, and the outlet or collecting chamber communicates with the exterior thereof. Before the filter is used, the moisture content of the hollow fibres is below 0.1 %, preferably below 0.05 %. In a separation method for removing particles from a particle-laden volume of liquid by means of such a filter, a pressure difference is generated between the interior and the exterior of the hollow fibres when the liquid is supplied to the filter, thus increasing the yield of permeate and reducing the filtering time. The total area of the hollow fibres is dimensioned such that a major part of the maximum permeate volume available can be obtained when the liquid flows once along the entire length of the hollow fibres, so that the filter can be discarded after a single use.



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DISPOSABLE FILTER AND SEPARATION METHOD USING THIS FILTER

This invention generally relates to a disposable filter comprising a bundle of hollow fibres arranged in a housing having an inlet for a particle-laden volume of liquid to be filtered, as well as an outlet or a collecting chamber for the permeate, said inlet communicating with the interior of the hollow fibres, and said outlet or collecting chamber communicating with the exterior thereof. The invention particularly concerns such a disposable filter for separating blood cells from whole blood.

Also, the invention generally relates to a separation method for removing small particles from a restricted volume of liquid. More precisely, the invention concerns a separation method for removing particles, such as cells, from a particle-laden volume of liquid by means of a filter comprising a bundle of hollow fibres arranged in a housing having an inlet for said liquid, as well as an outlet or a collecting chamber for the permeate, the total area of said hollow fibres being dimensioned for maximum exploitation the once the disposable filter is used, said inlet communicating with the interior of the hollow fibres, and said outlet or collecting chamber communicating with the exterior thereof, a pressure difference being generated between the interior and the exterior of said fibres when the volume of liquid is supplied to the filter, thus increasing the yield of permeate and reducing the filtering time. The invention particularly concerns such a method for separating blood cells from whole blood.

In many situations, it is necessary to remove small particles from a liquid in order that the separated, pure liquid might serve its purpose. One prior art separation technique is filtering, by which relatively large, non-elastic particles are effectively removed. However, prior art filtering techniques for separating small, elastic particles are not up to the mark as to single use and restricted volumes of liquid. In particular, there are no

disposable filters suited for very small volumes (in the order of e.g. 0.1-10 ml), for example when separating blood cells from whole blood, and when quantitative analysis of the permeate is required.

Thus, the present invention aims at providing a separation method and a device for implementing this method, both using a hollow-fibre filter and meeting the following requirements.

First, the filter should be disposable and therefore inexpensive, which necessitates simplicity of construction.

Second, the filter should be compact for easy manual handling.

Third, the filtering time should be very short, for example some ten seconds.

Fourth, the filter should give a high yield, i.e. as much permeate as possible, especially when the volumes of liquid are small. The yield should be at least 25%, as based on the volume of the liquid to be filtered. Of course, the filtering time mentioned above is the time needed for obtaining such a high yield.

Fifth, the particles to be removed, especially cells, must not be decomposed during filtering, since this would entail that parts of the particles might pass the filter.

Lastly, the permeate should allow a sufficiently accurate quantitative analysis. Thus, the concentrations of different substances in the permeate should essentially correspond to the concentrations in the original particle-laden liquid, the particle content thereof excluded.

The prior art embraces a multitude of differently designed filters using one or more hollow fibres. These filters are either continuous, in which case they are, for obvious reasons, unsuitable for the purpose of this invention, or disposable filters.

EP-A-0,315,252, for instance, discloses a disposable filter comprising hollow fibres. In this filter, the liquid to be filtered is passed over the exterior of a

hollow fibre which, to enable a sufficient yield, must be surrounded by a tube or the like, to produc a feed channel which is narrow enough. This construction unavoidably becomes very complicated if a large number of hollow fibres are used in order to obtain the large filter surface necessary for producing a considerable yield in a short time. Further, this filter is only suited for qualitative analysis of the different components of the permeate.

DE-A1-3,608,062 also discloses a disposable filter with a single hollow fibre. This filter is comparable with that of EP-A-0,315,252.

It is true that there are prior art filters which use hollow fibres and in which the liquid to be filtered is, in accordance with the invention, supplied to the interior of the fibres, but none of these existing filters satisfy the above requirements for the inventive filter. The main advantage of supplying the liquid to be filtered to the interior of the hollow fibres is that a sufficiently thin layer of liquid can be applied to the filter surface, thereby enabling effective filtering without any additional means. As a result, it is possible to obtain a high ratio of total filtering area to total filter volume, a ratio which is of decisive importance to the compactness of the filter.

According to the invention, the above requirements are met by a disposable filter of the type mentioned in the introduction to this specification and characterised in that the filter is hermetically sealed before use, and that the moisture content of said hollow fibres is lower than about 0.1%, preferably lower than about 0.05%.

This filter can be made compact and, by suitable dimensioning of the hollow fibres, be given a total filtering area so as to obtain the desired yield and filtering time, while avoiding particle decomposition. Especially, this filter enables quantitative analysis

owing to the very low moisture content, i.e. the low liquid content.

As will be described in more detail below, conventional hollow fibres regarded as dry have a moisture content which, when the fibres are used in a disposable filter for filtering relatively small volumes of liquid, have a diluting effect on the permeate, causing a quantitative analysis thereof to give incorrect results as to the concentrations of analysed substances in the original volume of liquid.

It should be observed that the hollow fibres used in filters normally have a quite significant moisture content in order to prevent damage to the hollow fibres and enable rapid start of the filtering operation, which usually requires wetting of the hollow fibre proper. The low moisture content according to the invention does not, however, cause any damage to the hollow fibres since the fibres are not dried until after having been mounted in the filter.

Tests on hollow fibres consisting of cellulose acetate and having a moisture content of 2% (glycerol in aqueous solution) gave the following results when whole blood to which iodine had been added was used as testing liquid and permeate samples were taken at regular intervals of 30 sec.

Samples	Iodine (mg/ml)
1	1.318
2	1.452
3	1.589

The corresponding samples taken upon centrifuging showed the following results.

Samples	Iodine (mg/ml)
1	1.735
2	1.699
3	1.660

An acceptable value is the mean value (1.698) with a deviation of ±4%, which thus is attained by the centrifuging tests but not the filter tests.

Similar tests on other filter materials give corresponding results. To achieve satisfying results, a moisture content according to the invention is required. In tests, such results have been attained also for natural blood components, such as bilirubin, albumin, LDH, iron and potassium, when using filter materials like polysulfone, cellulose triacetate and polyvinyl alcohol.

Owing to the very low moisture content of the fibres according to the invention, fibres of hydrophilic material are preferred since the filtering time otherwise tends to be too long.

Tests using a very hydrophobic filter material, such as polycarbonate, and involving whole blood and a pressure difference of 0.5 bar, show that wetting of the filter material requires more than three minutes. A hydrophilic material, such as polysulfone, is wet through in 30 sec, and a very hydrophilic material, e.g. polyvinyl alcohol, is wet through in 15-20 sec.

According to the invention, it is moreover desirable that the cross-sectional area of the pores of the hollow fibres increases from the interior of the fibres to the exterior, because such pores give, at a certain pressure difference across the fibre wall, the desired yield in a shorter time than pores of a substantially constant cross-sectional area corresponding to the smallest cross-sectional area of the pores preferred according to the invention. Alternatively, this property may be used for lowering the pressure difference, thereby reducing the risk of decomposition of the particles in the liquid to be filtered.

In a preferred embodiment of the invention, the disposable filter comprises a chamber for collecting the residue, said chamber communicating with the interior of the hollow fibres furthest away from the inlet in the longitudinal direction of said fibres. Suitably, this chamber is vented by means of at least one hollow fibre not used for the filtering. Especially, this residue-collecting

chamber is formed of a part of the inner volume of the hollow fibres situated furthest away from the inlet in the longitudinal direction of said fibres.

To prevent decomposition of the particles to be removed, especially cells, also the interior surface of the hollow fibres is treated to reduce the friction against the particles of the liquid and/or to increase biocompatibility.

To prevent premature clogging of the pores of the hollow fibres, the largest pore openings on the inside of the fibres should be smaller than about 1/5, preferably 1/10, of the size of the smallest particles to be removed from the liquid.

In an especially preferred embodiment of the disposable filter according to the invention, the space between and around the hollow fibres in the housing may, to reduce the filtering time, be filled with a hydrophobic material, e.g. microspheres, permitting the passage of liquid.

It should be emphasised that the disposable filter and the method according to the invention are particularly suited for separating blood corpuscles from whole blood, i.e producing blood plasma as permeate. Blood plasma, which comprises all the components of whole blood, with the exception of the red and white blood corpuscles, is today an important source for determining the health of humans and animals. Large-scale plasma separation is used in biochemical technique, and is of great importance in the medical service. In analysing technology, small sample volumes of plasma (0.001-5.0 ml) are generally desired, since this reduces the strain on the patient and involves a lower consumption of reagent for analysis. At present, plasma is separated from whole blood mainly by centrifuging, which is a laborious and time-consuming procedure. By manually separating plasma from whole blood in a closed disposable system in accordance with the invention, a reliable and highly expedient method of working is

obtained, which furthermore effectively prevents the operator from coming into contact with the patient's blood.

Although the invention is particularly suitable for separating blood plasma from whole blood, the requisite pressure difference being in the range of 0.05-0.5 bar, preferably 0.1-0.3 bar, it is by no means restricted to this application, but may be used for many other purposes, especially in medicine, chemistry, microbiology, micrology and biochemistry.

Suitably, the pressure difference is, at least partly, generated by producing a negative pressure in the housing before the liquid is supplied, by manually applying a positive pressure to the inlet, and/or by applying a negative pressure to the outlet. To avoid hemolysis, it is essential that the pressure difference across the walls of the hollow fibres is confined to a given value within the above-mentioned range. For this purpose, the disposable filter may be equipped with a pressure relief valve ensuring the necessary restriction of the pressure difference. Alternatively, the inlet of the filter may have a throttle restricting the flow rate through the inlet, thereby indirectly restricting the pressure difference.

It should be pointed out that the maximum pressure difference allowed depends on the ratio of the size of the smallest particles to be separated, to the size of the pore openings on the interior side of the hollow fibres. Naturally, the fact that the particles may be elastic, which makes the smallest diameter variable, is also of importance, as is the fact that the pores may have a constant cross-sectional area or a cross-sectional area increasing towards the exterior of the hollow fibres.

The invention will now be described in more detail below, reference being had to the accompanying drawings, in which

Fig. 1 is a side view showing a partly cut open first embodiment of a disposable filter according to the invention,

Fig. 2A is a longitudinal section and Fig. 2B a cross-section of a second embodiment of a disposable filter according to the invention, and

Fig. 3 is a schematic, much enlarged longitudinal section of a hollow fibre of the type used in the inventive disposable filter.

The embodiment of Fig. 1 comprises a housing 1 made up of a cylindrical sleeve 2 whose upper end is closed by an inlet lid 3 with an inlet tube 4 and whose lower end is closed by a residue lid 5. Immediately above the lid 5, an outlet tube 6 is fitted on the sleeve 2. A bundle of hollow fibres 7 extend axially through the sleeve 2 and are, at the upper sleeve end, fitted into a sealing plug 8 in such a manner that the inlet tube communicates with the interior of the fibres, at the upper end thereof. The lower ends of the hollow fibres 7 are fitted into a second sealing plug 9 provided at the lower end of the sleeve 2, in such a manner that a residue chamber 10 formed between the sealing plug 9 and the bottom of the residue lid 5 communicates with the interior of the hollow fibres, at the lower end thereof. The outlet tube 6 communicates with the space around the hollow fibres 7 inside the sleeve 2. The total filter area of the hollow fibres is dimensioned such that a major part of the maximum permeate volume available can be obtained when the liquid flows once along the entire length of the hollow fibres, so that the filter can be discarded after a single use.

At least one hollow fibre 7' is closed at its upper end, and the interior of this fibre 7' thus does not communicate with the inlet tube 4, but with the residue chamber 10 for venting of the latter.

When a particle-laden volume of liquid is supplied through the inlet tube 4 to the disposable filter of Fig. 1, a pressure difference is generated between the inlet 4 and the outlet 6. This may be achieved in different ways, for example by manually applying a positive pressure to the inlet, by applying a negative pressure to

the outlet, for instance by means of a so-called vacutainer, and/or by generating a negative pressure in the housing 1 before the liquid is supplied. Thus, the liquid will flow axially through the interior of the hollow fibres 7 from the inlet tube 4 towards the residue chamber 10. While this happens, those particles unable to pass through the fibre walls will move towards the residue chamber 10, whereas the liquid proper will pass through the fibre walls and flow to the outlet tube 6 which communicates with a container (not shown) for collecting the permeate. Naturally, the residue chamber 10 should be dimensioned with due regard to the expected volume of residue or the amount thereof which is to be contained in the residue chamber.

The embodiment of Figs 2A and 2B mainly differs from that of Fig. 1 in that the bundle of hollow fibres 7 is doubled, so that all the fibre ends are fitted into one and the same sealing plug 11. In this case, the housing 1' is formed of a cylindrical sleeve 2' whose one end is closed with the exception of an outlet tube 6' and whose other end is closed by an inlet lid 3'. Between the lid 3' and the sealing plug 11, a partition 12 is arranged in such a manner that one end of the hollow fibres 7 is situated on one side of the partition 12, and the other end of the hollow fibres 7 is situated on the other side of this partition. Further, the inlet lid 3' is equipped with an inlet tube 4'. Like the embodiment of Fig. 1, the embodiment of Fig. 2 comprises at least one hollow fibre 7' which is closed at the end facing the inlet tube 4'. A residue chamber 10' is formed between the inlet lid 3' and the sealing plug 11, on the side of the partition 12 where the inlet tube 4' is not arranged.

In both the embodiment of Fig. 1 and that of Figs 2A and 2B, a vent tube 13; 13' is suitably connected to the upper part of the sleeve 2; 2'. Advantageously, the tube 13; 13' is equipped with a nonreturn valve permitting nothing but air to leave the housing 1; 1'.

The cross-section in Fig. 3 of a hollow fibre 7 illustrates the filtering procedure in a disposable filter according to the invention. When using this filter to separate blood plasma from whole blood, the total filter area of the hollow fibres 7 should be 10-100 cm^2/ml of whole blood, preferably 20-80 cm^2/ml. Further, the hollow fibres should have an internal diameter of 0.10-0.40 mm, preferably 0.15-0.30 mm, and a wall thickness of 0.001-0.150 mm, preferably 0.050-0.100 mm. Moreover, the size of the fibre pores on the surface communicating with the inlet should be 0.05-0.7 µm, preferably 0.1-0.3 µm, and the porosity should be 60-95%. These values have been established in view of the fact that the red and white blood corpuscles constitute about 45% by volume of whole blood. Generally speaking, the invention is especially suitable for liquids in which the particles to be removed make up at least about 10% by volume of the total liquid. This requires a filter area of 5-100 cm^2/ml of liquid, preferably 15-50 cm^2/ml of liquid.

As indicated in Fig. 3, the smallest opening area of the pores 14 in the fibre walls should be situated closest to the surface communicating with the inlet, i.e. closest to the interior of the hollow fibres 7.

The passage of the liquid through the hollow fibre 7 and that of the permeate through the fibre walls are indicated by arrows 15 in Fig. 3. For the liquid, the yield, i.e. the relative proportion of the liquid that rid of particles passes through the fibre walls, is at its largest at the beginning of the procedure. As time goes on, the yield decreases as a result of the increasing concentration of particles closest to the interior of the fibre walls, and the clogging of some of the pores 14. This also augments the risk of particles decomposing owing to contact with or friction against the interior of the fibre walls, which may aggravate the clogging of the pores

14, but also lead to the presenc of parts of particles in the permeate, which is highly undesirable.

In the case of whole blood, the contact with or the friction against the inside of the hollow fibre 7 involves the risk of hemolysis. With the invention, this risk is considerably reduced in that the inside of the fibre 7 is made biocompatible, e.g. by heparinisation or sulphating.

The heparinisation or sulfating thus contributes to increase the flow through the fibre walls, thereby augmenting the yield and/or reducing the filtering time required.

Suitable fibre materials include polypropylene, polyvinyl alcohol, cellulose acetate, polyamide, polysulfone, polyacrylonitrile, and fluorinated polymers.

To shorten the filtering time, it is furthermore essential that the dead volume in the housing, i.e. the difference between the total inner volume of the housing and the volume of the hollow fibres in the housing, is as small as possible. According to the invention, the dead volume can be reduced by filling the space between and around the hollow fibres in the housing with a hydrophobic material permitting the passage of liquid. Such a material suitably consists of glass microspheres having a diameter in the order of e.g. 200-500 µm. By filling this space with such microspheres, the dead volume can be reduced to e.g. 10-30% of the total inner volume of the housing. In other words, the hollow fibres in an inventive disposable filter will take up at least 65% of the internal cross-sectional area of the housing; including the microspheres about 90% will be taken up. Thus, Figs 1 and 2A, which only show a few fibres, are very schematic, and in actual practice the fibres are packed quite close together.

Several modifications of the above embodiments are conceivable within the scope of the invention, as indicated in the appended claims.

For instance, the outlet may communicate with a permeate-collecting chamber joined to the filter. In the embodiment of Fig. 2, the outlet 6' may even be left out, and the sleeve 2' may also form a permeate-collecting chamber. Optionally, the sleeve 2' is extended downwards, beyond the lowermost parts of the hollow fibres 7, 7' to form a permeate-collecting chamber entirely or partly separated from the space taken up by the hollow fibres.

When a permeate-collecting chamber is joined to or integrated with the filter, the subsequent analysis of the permeate may, in some applications, be carried out without removing the chamber from the filter. However, it should suitably be possible to separate the permeate chamber from the rest of the filter. Especially, the permeate chamber may be a known spectrophotometric cuvette. Chemical substances, e.g. colour reagents and/or enzymes, reagent strips or the like, may be provided in advance in the cuvette, thus enabling direct analysis of the filtrate without further handling thereof.

Moreover, the inlet may be integrated or otherwise connected with a hypodermic needle. The different inlets and outlets of the filter may initially be closed by, for instance, a membrane which can be penetrated by e.g. a hypodermic needle. Also other closing means are conceivable, albeit not shown in the embodiments described which, by the way, do not comprise any means for restricting the pressure difference across the fibre walls. However, such means are obvious to the expert.

CLAIMS

1. A disposable filter comprising a bundle of hollow fibres (7) arranged in a housing (1; 1') having an inlet (4; 4') for a particle-laden volume of liquid to be filtered, as well as an outlet (6; 6') or a collecting chamber for the permeate, said inlet communicating with the interior of the hollow fibres, and said outlet or collecting chamber communicating with the exterior thereof, c h a r a c t e r i s e d in that the filter is hermetically sealed before use, and that the moisture content of said hollow fibres (7) is lower than about 0.1%, preferably lower than about 0.05%.

2. The disposable filter of claim 1, c h a r a c t e r i s e d in that the hollow fibres (7) consist of a hydrophilic material.

3. The disposable filter of claim 1 or 2, c h a r a c t e r i s e d in that the cross-sectional area of the pores (14) of the hollow fibres (7) increases from the interior of said fibres to the exterior thereof.

4. The disposable filter of any one of claims 1-3, c h a r a c t e r i s e d by a chamber (10; 10') for collecting the residue, said chamber communicating with the interior of the hollow fibres (7) furthest away from the inlet (4; 4') in the longitudinal direction of said hollow fibres and being vented by means of at least one hollow fibre (7') not used for the filtering.

5. The disposable filter of claim 4, c h a r a c t e r i s e d in that the residue-collecting chamber is formed of a part of the inner volume of the hollow fibres (7) situated furthest away from the inlet (4; 4') in the longitudinal direction of said fibres.

6. The disposable filter of any one of claims 1-5, c h a r a c t e r i s e d in that the interior surface of the hollow fibres (7) is treated to reduce the friction

against the particles of the liquid and/or to increase biocompatibility.

7. The disposable filter of any one of claims 1-6, c h a r a c t e r i s e d in that the size of the openings on the inside of the hollow fibres (7) is approximately 1/5, preferably 1/10, of the size of the smallest particles to be removed from the liquid.

8. The disposable filter of any one of claims 1-7, c h a r a c t e r i s e d in that the space between and around the hollow fibres in the housing (1; 1') is filled with hydrophobic material, preferably microspheres, permitting the passage of liquid.

9. The disposable filter of any one of claims 1-8, c h a r a c t e r i s e d in that there is a negative pressure in the housing (1; 1') before the filter is used.

10. The disposable filter of any one of claims 1-9, for separating blood plasma from whole blood, c h a r a c t e r i s e d in that the total inner filter area of the hollow fibres (7) is 10-100 cm^2/ml of whole blood to be filtered, preferably 20-80 cm^2/ml of whole blood.

11. The disposable filter of claim 10, c h a r a c t e r i s e d in that the hollow fibres (7) have a pore diameter of 0.05-0.7 µm, preferably 0.1-0.3 µm, on the interior, and a porosity of 60-95%.

12. The disposable filter of claim 10 or 11, c h a r a c t e r i s e d in that the hollow fibres (7) have an internal diameter of 0.10-0.40 mm, preferably 0.15-0.30 mm, and a wall thickness of 0.001-0.150 mm, preferably 0.05-0.10 mm.

13. The disposable filter of any one of claims 10-12, c h a r a c t e r i s e d in that the inside of the hollow fibres (7) is heparinised or sulphated.

14. The disposable filter of any one of claims 1-13, c h a r a c t e r i s e d by a pressure relief valve confining the pressure difference across the walls of the hollow fibres (7) to a given value.

against the particles of the liquid and/or to increase biocompatibility.

7. The disposable filter of any one of claims 1-6, c h a r a c t e r i s e d in that the size of the openings on the inside of the hollow fibres (7) is approximately 1/5, preferably 1/10, of the size of the smallest particles to be removed from the liquid.

8. The disposable filter of any one of claims 1-7, c h a r a c t e r i s e d in that the space between and around the hollow fibres in the housing (1; 1') is filled with hydrophobic material, preferably microspheres, permitting the passage of liquid.

9. The disposable filter of any one of claims 1-8, c h a r a c t e r i s e d in that there is a negative pressure in the housing (1; 1') before the filter is used.

10. The disposable filter of any one of claims 1-9, for separating blood plasma from whole blood, c h a r a c t e r i s e d in that the total inner filter area of the hollow fibres (7) is 10-100 cm^2/ml of whole blood to be filtered, preferably 20-80 cm^2/ml of whole blood.

11. The disposable filter of claim 10, c h a r a c t e r i s e d in that the hollow fibres (7) have a pore diameter of 0.05-0.7 µm, preferably 0.1-0.3 µm, on the interior, and a porosity of 60-95%.

12. The disposable filter of claim 10 or 11, c h a r a c t e r i s e d in that the hollow fibres (7) have an internal diameter of 0.10-0.40 mm, preferably 0.15-0.30 mm, and a wall thickness of 0.001-0.150 mm, preferably 0.05-0.10 mm.

13. The disposable filter of any one of claims 10-12, c h a r a c t e r i s e d in that the inside of the hollow fibres (7) is heparinised or sulphated.

14. The disposable filter of any one of claims 1-13, c h a r a c t e r i s e d by a pressure relief valve confining the pressure difference across the walls of the hollow fibres (7) to a given value.

15. The disposable filter of any one of claims 1-13, c h a r a c t r i s e d in that the inlet (4; 4') has a throttle for restricting the flow rate through said inlet.

16. A separation method for removing particles from a particle-laden volume of liquid by means of a filter comprising a bundle of hollow fibres arranged in a housing having an inlet for said liquid, as well as an outlet or a collecting chamber for the permeate, the total area of said hollow fibres being dimensioned for maximum exploitation the once the disposable filter is used, said inlet communicating with the interior of the hollow fibres, and said outlet or collecting chamber communicating with the exterior thereof, a pressure difference being generated between the interior and the exterior of said fibres when the volume of liquid is supplied to the filter, thus increasing the yield of permeate and reducing the filtering time, c h a r a c t e r i s e d in that the moisture content of said hollow fibres is reduced to at least 0.1%, preferably at least 0.05%, before use, and that the filter is then hermetically sealed.

17. The method of claim 16, c h a r a c t e r i s e d in that the liquid is prefiltered in order to remove particles more than five times as large as the smallest particles to be filtered out.

18. The method of claim 16 or 17, for separating blood corpuscles from whole blood, c h a r a c t e r i s e d in that, upon filtration, a pressure difference of 0.05-0.5 bar, preferably 0.1-0.3 bar, is generated across the fibre walls of a filter having hollow fibres with a wall thickness of 0.001-0.150 mm, preferably 0.05-0.10 mm, and an internal diameter of 0.10-0.40 mm, preferably 0.15-0.30 mm.

FIG_1

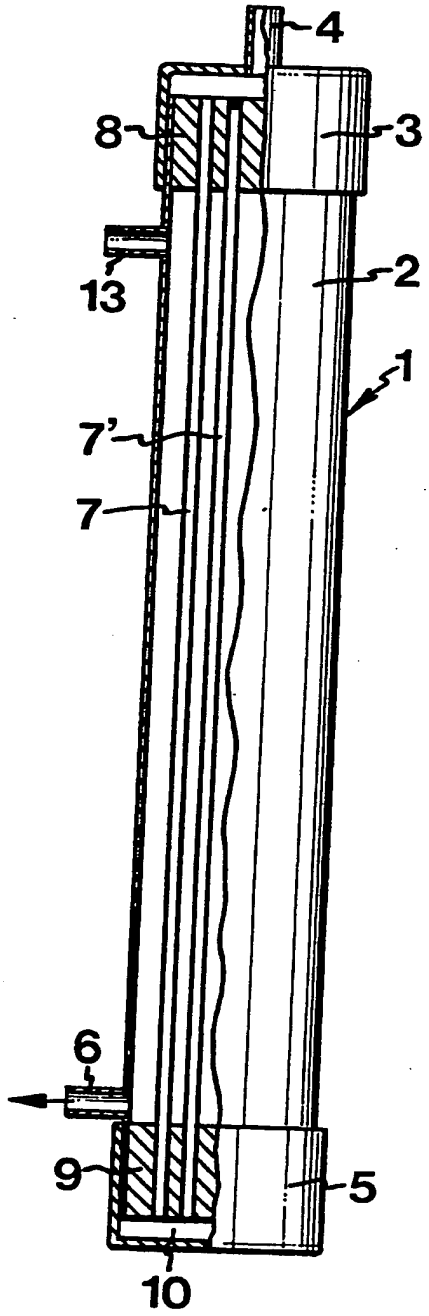


FIG_2A

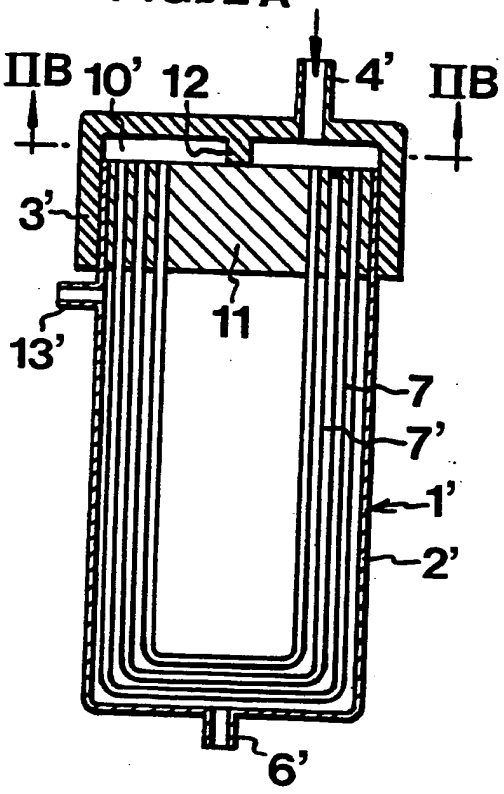


FIG_2B

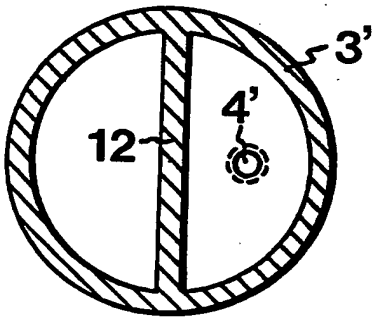
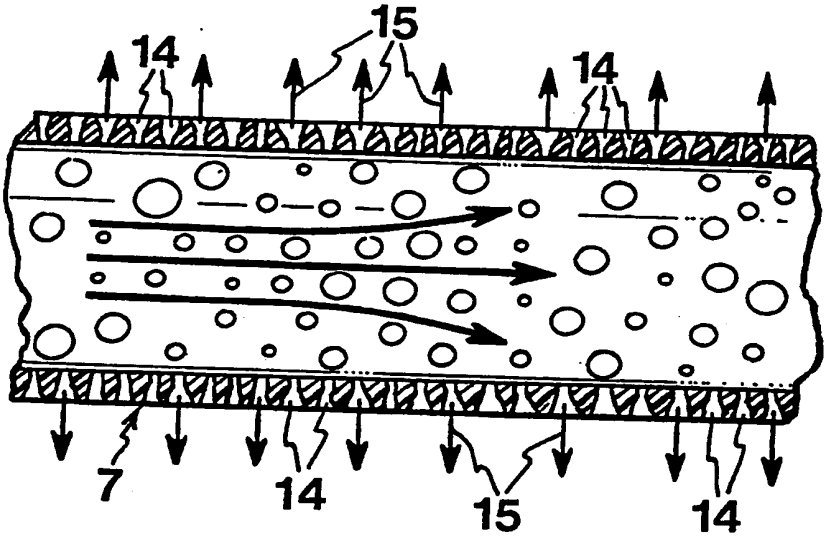


FIG_3



INTERNATIONAL SEARCH REPORT

International Application No PCT/SE 90/00811

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)[6]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC5: A 61 M 1/34, B 01 D 61/18

II. FIELDS SEARCHED

Minimum Documentation Searched[7]

Classification System	Classification Symbols
IPC5	A 61 M; B 01 D; G 01 N

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in Fields Searched[8]

SE,DK,FI,NO classes as above

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

Category *	Citation of Document,[11] with indication, where appropriate, of the relevant passages[12]	Relevant to Claim No.[13]
A	EP, A1, 0315252 (AKZO N.V.) 10 May 1989, see the whole document --	1-18
A	EP, A2, 0219053 (AMERICAN HOSPITAL SUPPLY CORPORATION) 22 April 1987, see the whole document --	1-18
A	EP, A2, 0229388 (FRESENIUS AG) 22 July 1987, see the whole document --	1-18
A	EP, A2, 0184852 (BECTON, DICKINSON AND COMPANY) 18 June 1986, see the whole document --	1-18

* Special categories of cited documents: [10]

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
20th February 1991	1991 -02- 25
International Searching Authority	Signature of Authorized Officer
SWEDISH PATENT OFFICE	Inger Löfgren

Form PCT/ISA/210 (second sheet) (January 1985)

III. DOCUMENTS CONSIDERED T BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
A	US, A, 4267053 (YASUO HASHINO ET AL) 12 May 1981, see the whole document --	1-18
A	US, A, 4707268 (DILIP H. SHAH ET AL) 17 November 1987, see the whole document --	1-18
A	DE, A1, 3636583 (DRÄGERWERK AG) 5 May 1988, see the whole document --	1-18

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO.PCT/SE 90/00811

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the Swedish Patent Office EDP file on 91-01-31 The Swedish Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
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		WO-A-	84/01522	84-04-26
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		US-A-	4840227	89-06-20